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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/712,813	11/13/2000	Gale A. Granger	IRVN-007CON	4642

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EXAMINER	
MURPHY, JOSEPH F	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 12/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	09/712,813	GRANGER ET AL.	
	Examin r	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-75* is/are pending in the application.

4a) Of the above claim(s) *67-69,74 and 75* is/are withdrawn from consideration.

5)☒ Claim(s) *57-66* is/are allowed.

6)☒ Claim(s) *43-45 and 47* is/are rejected.

7)☒ Claim(s) *46,48-56 and 70-73* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Formal Matters

Claims 43-75 are pending. Claims 67-69 stand withdrawn from consideration pursuant to 37 CFR 1.142(b). Newly presented claims 74-75 are also withdrawn as being drawn to a non-elected invention, as they read on the pharmaceutical composition of claims 67-69. Claims 43-66, 70-73 are under consideration.

Response to Amendment

The rejections of claims 46, 48-66, 70-73 are withdrawn. Remaining issues are set forth below.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43-45, 47 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of sepsis, MS, arthritis, or reducing inflammation, by administration of SEQ ID NO: 8 or SEQ ID NO: 9, does not reasonably provide enablement for methods of treatment of arthritis or reducing inflammation by administration of any protein other than SEQ ID NO: 8 or 9; or treatment of any other inflammatory condition using any protein that releases TNF receptor, for reasons of record set forth in the Office Action of 9/8/2003. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not provide enablement for methods of treatment of arthritis or reducing inflammation by administration of any protein other than SEQ ID NO: 8 or 9; or treatment of any other inflammatory condition using any protein that releases TNF receptor. Claims 43-45, 47 are overly broad since insufficient guidance is provided as to which of the myriad of encompassed polypeptides that will retain the characteristics of TRRE activity. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue.

Applicant argues that the claims are in compliance with the requirements of 35 USC § 112 by defining the protein according to its function. This is explicitly permitted under § 112 paragraph 6. Applicant also argues that the protein means that causes TNF receptor to be released from the surface of cells is illustrated in the specification not only as the proteins encoded in SEQ. ID NOs:8 and 9, their fragments and variants, but also by proteins encoded in SEQ. ID NOs:1 to 7 and SEQ. ID NO:9. Protein expressed from SEQ. ID NOs: 4 and 6 are shown to prevent septic shock in Example 6. However as set forth in MPEP 2181, a claim limitation will be interpreted to invoke 35 U.S.C. 112, sixth paragraph if it meets the following 3-prong analysis: (A) the claim limitations must use the phrase "means for" or "step for"; (B) the "means for" or "step for" must be modified by functional language; and (C) the phrase "means for" or "step for" must not be modified by sufficient structure, material or acts for achieving the specified function. With respect to the first prong of this analysis, a claim element that does not include the phrase "means for" or "step for" will not be considered to invoke 35 U.S.C. 112, sixth paragraph. In the instant case the claims do not recite the phrase "means for" or "step for", and therefore do not invoke the analysis under 112 sixth paragraph.

Applicant further argues that the specification provides a system by which the reader may obtain and test other proteins to determine if they cause release of TNF receptors according to the invention. Example 1 describes an assay system in which a protein is tested for its ability to release TNF receptor from a cell line transfected to express TNF receptors in a high density and stable fashion. However, claims 43-45 are overly broad because they define a polypeptide used in the method by a function alone, i.e. the polypeptide causes TNF receptor to be cleaved. However, in Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991), the court ruled that a claim to a large genus of possible genetic sequences encoding a protein with a particular function that needs to be determined subsequent to the construction of the genetic sequences may not find sufficient support under 35 USC 112, 1st paragraph, if only a few of the sequences that meet the functional limitations of the claim are disclosed and if undue experimentation would be required of one skilled in the art for determining other genetic sequences embraced by the claim. In the instant case, there are no structural features set forth for the polypeptide that must have the function of cleaving TNF receptor, thus it would require undue experimentation for one of skill in the art to determine which polypeptides, given no structural information, would retain the function of cleaving TNF receptor.

In addition, the instant claims are directed to methods for treating an inflammatory condition with SEQ ID NO: 8 or 9. The Specification exemplifies alleviation of sepsis (Specification at 37) by administration of SEQ ID NO: 8 or 9, while the claims encompass the treatment of any and all inflammatory conditions. Applicant argues that the disclosure provides a full description of the importance of the TNF pathway in mediating inflammatory reactions, and the potential for treating inflammatory conditions by preventing TNF receptor transduction

using the receptor releasing proteins of this invention. Examples 2 and 6 illustrate the treatment methods of the invention in an animal model for septic shock. Applicant argues the specification is enabling for the treatment of all other inflammatory conditions, because the formulation and administration of the therapeutic agent for other conditions can follow the same procedure as in the septic shock model, or adapted to the condition in accordance with standard protocols known in the art of preparing biological agents for therapeutic administration. Applicant has also provided a written presentation prepared by Meyer Pharmaceuticals that demonstrates the treatment of septic shock, arthritis and the mouse EAE model of MS. However, the claims encompass the treatment of any and all inflammatory conditions, while the specification has only taught methods for treating sepsis. The sepsis model is not a model for any and all inflammatory conditions, nor are the arthritis and EAE models cited in the presentation. Furthermore, any analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to practice the claimed invention. Here, the Specification did not contain the disclosure of the claimed method functioning in the arthritis and EAE models, and as above, these models are not indicative of all inflammatory conditions. Since Applicant is required to enable one of skill in the art to practice the claimed invention, while the claims encompass methods that the skilled artisan would need to determine the effect of the claimed method of administration on all inflammatory conditions, while the specification only demonstrates the effect on sepsis, and the written presentation shows the effect in arthritis and EAE models, but after the time if filing. It would require undue experimentation for one of skill in the art to practice the claimed method, since the skilled artisan

would have to first determine the nexus between the demonstrated treatment of sepsis and the treatment of all inflammatory conditions.

Claims 43-45 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in the Office Action of 9/8/2003. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The rejection of record set forth that these are genus claims. The claims are drawn to methods of treatment of arthritis or rheumatoid arthritis by administration of SEQ ID NO: 8 or 9; methods of treatment of septic shock, arthritis or rheumatoid arthritis by administration of any protein; methods of treatment of septic shock, arthritis or rheumatoid arthritis by administration by administration of proteins which comprise fragments of SEQ ID NO: 8 or 9; methods of treatment of septic shock, arthritis or rheumatoid arthritis by administration by administration of proteins which are 80% or 95% identical to SEQ ID NO: 8 or 9. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions

and/or additions that may be made to SEQ ID NO: 8 or 9, and additionally encompass administration of a protein defined by a function alone i.e. cleaving and releasing TNF receptor. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the polypeptide of SEQ ID NO: 8 or 9 is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Applicant argues that the specification provides a system by which the reader may obtain and test other proteins to determine if they cause release of TNF receptors according to the invention. Example 1 describes an assay system in which a protein is tested for its ability to release TNF receptor from a cell line transfected to express TNF receptors in a high density and stable fashion. However, in University of California v. Eli Lilly, 119 F.3 at 1568, 43 USPQ2d at 1406. the Court decided that a definition by function alone "does not suffice" to sufficiently describe a biomolecule "because it is only an indication of what the gene does, rather than what it is." Further, "it is only a definition of a useful result rather that a definition of what achieves

that result...The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention". *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). While Applicant has set forth a method for obtaining a polypeptide which causes TNF receptor to be cleaved, Applicant has not set forth within the claim the detailed constitution of the this polypeptide, and thus does not satisfy the written description requirement.

Conclusion

Claims 43-45, 47 are rejected.

Claims 46, 48-56, 70-73 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 57-66 are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
December 9, 2003

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SUPERVISORY PATENT EXAMINER
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